Maxrin® D

Tamsulosin Hydrochloride USP 0.4 mg & Dutasteride USP 0.5 mg

Composition

Each capsule contains blended pellets of Tamsulosin Hydrochloride USP 0.4 mg & Dutasteride USP 0.5 mg.

Pharmacology

Tamsulosin & Dutasteride is a combination of two drugs with complementary mechanisms of action to improve symptoms in patients with Benign Prostatic Hyperplasia (BPH). Tamsulosin Hydrochloride, an antagonist of alpha$_{1A}$-adrenoreceptors and Dutasteride, a dual 5 alpha reductase inhibitor (5ARI).

Treatment of BPH with alpha$_1$-adrenoreceptor blocking agents and 5ARIs results in an improvement in urine flow rate and a reduction in symptoms of BPH.

Tamsulosin: An alpha$_1$-adrenoreceptor blocking agent that affects the dynamic component of BPH by inhibiting alpha$_1$-adrenoreceptors in the stromal prostatic smooth muscle and bladder neck. Blockade of these adrenoreceptors can cause smooth muscles in the bladder neck and prostate to relax. Specifically, Tamsulosin exhibits selectivity for both alpha$_{1A}$ and alpha$_{1D}$ receptors over the alpha$_{1B}$ adrenoreceptor subtype. These three adrenoreceptor subtypes have a distinct distribution pattern in human tissue. Whereas approximately 70% of the alpha$_1$-receptors in human prostate are of the alpha$_{1A}$ subtype, the human bladder contains predominantly the alpha$_{1D}$ subtype while blood vessels express predominantly alpha$_{1B}$ subtype. It is further believed that blockade of the alpha$_{1D}$ subtypes in the human obstructed bladder may be responsible for reducing detrusor overactivity and subsequent relief of storage symptoms.

Dutasteride: A synthetic 4-azasteriod compound is a competitive and specific inhibitor of both Type I and Type II 5 alpha-reductase isoenzymes that affects the static component of BPH by inhibiting the conversion of Testosterone to Dihydrotestosterone (DHT) by the enzyme 5 alpha-reductase. 5 alpha-reductase exists as 2 isoforms, Type I and Type II, both of which are present in the prostate. It has been observed that compared to normal tissue, the expression of both isoenzymes are increased in BPH tissue. Dissociation from this complex has been evaluated under in vitro and in vivo conditions and is extremely slow. Dutasteride lowers DHT levels and leads to a reduction in prostatic volume, thereby treating an underlying cause of BPH. Dutasteride does not bind to the human androgen receptor.

Indication

Combination of Tamsulosin Hydrochloride & Dutasteride capsules are indicated for the treatment of moderate to severe symptomatic Benign Prostatic Hyperplasia (BPH) in men with enlarged prostates. Tamsulosin in combination with Dutasteride has been shown to reduce symptoms of BPH, improve urinary flow and reduce prostate size and was statistically significant to Tamsulosin monotherapy. Tamsulosin in combination with Dutasteride was statistically significant to Tamsulosin monotherapy but not Dutasteride monotherapy at reducing the relative risk of Acute Urinary Retention (AUR) or BPH-related surgery.

Dosage & Administration

Recommended Dose and Dosage Adjustment

Adult males (including geriatric patients): The recommended dose of combination is one capsule daily taken orally approximately 30 minutes after the same meal.

Although an improvement in symptoms may be observed after 3 months in some patients, it can take up to 6 months before a response to the treatment can be achieved.

Missed Dose: If a dose is missed, it can be taken later in the same day. Extra capsules taken for missed doses are not necessary. Do not take two doses in the same day.

Dosing considerations

Hepatic Insufficiency: Tamsulosin has not been studied in patients with severe hepatic dysfunction. Patients with mild to moderate hepatic dysfunction do not require an adjustment in Tamsulosin dosage. The effect of hepatic impairment on Dutasteride pharmacokinetics has not been studied. Caution should be used in the administration of Tamsulosin & Dutasteride to patients with liver disease.

Renal Insufficiency: Patients with renal impairment do not require an adjustment in Tamsulosin dosing. Patients with end stage renal disease (CrCl < 10 mL/min) have not been studied. No adjustment in dose is anticipated for patients with renal impairment. The effects of renal impairment on Dutasteride pharmacokinetics have not been studied. However, less than 0.1% of a steady-state 0.5 mg dose of Dutasteride is recovered in human urine, so no adjustment in dosage is anticipated for patients with renal impairment.

Contraindication

Combination of Tamsulosin & Dutasteride is contraindicated for use in women and children. It is contraindicated in patients with known hypersensitivity to Tamsulosin Hydrochloride (including Tamsulosin induced angioedema), Dutasteride (including other 5 alpha-reductase inhibitors) or to any ingredient in the formulation.

Adverse effects

The most common adverse reactions reported in subjects receiving combination therapy were impotence, decreased libido, breast disorders (including breast enlargement and tenderness), ejaculation disorders and dizziness. The percentages of subjects with ejaculation disorders, decreased libido and impotence were higher in the combination therapy group compared with either monotherapy groups.

Warning

Combination of Tamsulosin & Dutasteride is for use in men only. Women who are pregnant, or who may become pregnant, should not handle combination as it may pass through the skin. Combination may affect the normal development of the external genital organs in a male baby. As with all alpha$_1$-adrenoceptor antagonists, a reduction in blood pressure can occur in individual cases during treatment with Tamsulosin, as a result of which, there is a potential risk of syncope. At the first signs of orthostatic hypotension (dizziness, weakness), the patient should sit or lie down until the symptoms have disappeared. Do not use combination with other alpha adrenergic antagonists, as this may increase the risk of hypotension.

Do not use this combination with strong inhibitors of cytochrome P450 (CYP) 3A4 (e.g., Ketoconazole). Use caution in combination with moderate CYP3A4 inhibitors (e.g., Erythromycin) or strong (e.g., Paroxetine) or moderate CYP2D6 inhibitors, or known poor metabolizers of CYP2D6.

Men should not donate blood until at least 6 months have passed following their last dose of combination. The purpose of this deferred period is to prevent administration of Dutasteride to a pregnant female transfusion recipient.

Intraoperative Floppy Iris Syndrome: Intraoperative Floppy Iris Syndrome (IFIS, a variant of small pupil syndrome) has been observed during cataract surgery in some patients treated with alpha$_1$ adrenoreceptor blockers, including Tamsulosin.

Priapism: Priapism (persistent painful penile erection unrelated to sexual activity) has been associated (probably less than 1 in 50,000) with the use of alpha-adrenergic antagonists. This condition can lead to permanent impotence if not properly treated; patients must be advised about the seriousness of the condition.

Dutasteride is absorbed through the skin and therefore contact with leaking capsules must be avoided. If contact is made with leaking capsules, the contact area should be washed immediately with soap and water.

Drug Interactions

Strong Inhibitors of CYP3A4: Tamsulosin-containing products, including combination, should not be co-administered with strong CYP3A4 inhibitors (e.g., Ketoconazole) as this can significantly increase Tamsulosin exposure.

Inhibitors of CYP2D6 and Moderate Inhibitors of CYP3A4: Tamsulosin-containing products, including combination should be used with caution when co-administered with moderate inhibitors of CYP3A4 (e.g., Erythromycin), strong (e.g., Paroxetine) or moderate (e.g., Terbinafine) inhibitors of CYP2D6, or in patients known to be poor metabolizers of CYP2D6 as there is a potential for significant increase in Tamsulosin exposure.

Cimetidine: Caution is advised when Tamsulosin-containing products, including combination are co-administered with Cimetidine.

Other Alpha-adrenergic Antagonists: Tamsulosin-containing products, including combination should not be co-administered with other alpha-adrenergic antagonists because of the increased risk of symptomatic hypotension.

Phosphodiesterase-5 Inhibitors (PDE-5 Inhibitors): Caution is advised when alpha adrenergic antagonist-containing products, including combination, are co-administered with PDE-5 inhibitors. Alpha-adrenergic antagonists and PDE-5 inhibitors are both vasodilators that can lower blood pressure. Concomitant use of these 2 drug classes can potentially cause symptomatic hypotension.

Warfarin: Caution should be exercised with concomitant administration of Warfarin and Tamsulosin-containing products, including combination.

Use in Pregnancy and Lactation

Pregnancy: Combination of Tamsulosin & Dutasteride is contraindicated for use in women. There are no adequate and well-controlled studies in pregnant women of this combination or its individual components. Administration of Tamsulosin to pregnant female rats and rabbits at higher than the human therapeutic dose showed no evidence of fetal harm. The potential risk from the use of Tamsulosin during pregnancy in humans is unknown. Dutasteride has not been studied in women because pre-clinical data suggests that the suppression of circulating levels of Dihydrotestosterone may inhibit the development of the external genital organs in a male fetus carried by a woman exposed to Dutasteride.

Lactating Mother: This combination is contraindicated for use in women. It is not known whether Tamsulosin or Dutasteride are excreted in breast milk.

Pediatric Use

This combination is contraindicated for use in children. BPH is not a disease of childhood. Safety and effectiveness of Tamsulosin or Dutasteride in children have not been established.

Storage condition

Store in cool and dry place, protected from light. Keep out of the reach of children.

Package quantities

Box contains 20 capsules in blister pack.

Manufactured by

SQUARE
PHARMACEUTICALS LTD.
BANGLADESH